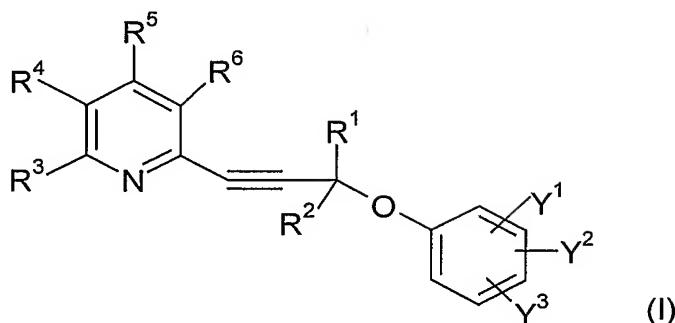


Claims

1. A compound of formula I



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wherein

R<sup>1</sup> is selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by C<sub>1</sub>-C<sub>4</sub> alkyl;

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R<sup>2</sup> is selected from hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>3</sup> is selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, F, CF<sub>3</sub>, CHF<sub>2</sub> and CH<sub>2</sub>F;

R<sup>4</sup> is selected from hydrogen, F, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F and CH<sub>3</sub>;

R<sup>5</sup> is selected from hydrogen and F;

R<sup>6</sup> is selected from hydrogen and F;

15

Y<sup>1</sup> is selected from hydrogen; halogen; nitrile; C<sub>1</sub>-C<sub>4</sub> alkoxy; C<sub>1</sub>-C<sub>4</sub> alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a

fluorine atom; benzyloxy; nitro in the meta or para position; and C<sub>1</sub>-C<sub>4</sub> alkyl ester;

Y<sup>2</sup> is selected from hydrogen; halogen; nitrile; C<sub>1</sub>-C<sub>4</sub> alkoxy; C<sub>1</sub>-C<sub>4</sub> alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a

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fluorine atom; and C<sub>1</sub>-C<sub>4</sub> alkyl ester;

Y<sup>3</sup> is selected from hydrogen; halogen; nitrile; C<sub>1</sub>-C<sub>4</sub> alkoxy; C<sub>1</sub>-C<sub>4</sub> alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a

fluorine atom; and C<sub>1</sub>-C<sub>4</sub> alkyl ester; or

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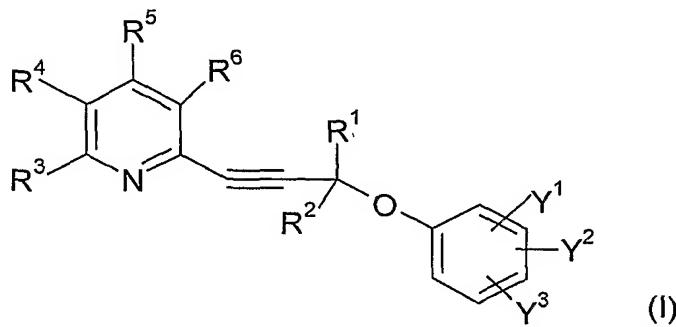
Y<sup>1</sup> and Y<sup>2</sup> may form an aromatic or non-aromatic ring, optionally substituted by halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl wherein one or more of the hydrogen

atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or C<sub>1</sub>-C<sub>4</sub> alkyl ester;

with the proviso that when Y<sup>1</sup> is hydrogen, Y<sup>2</sup> is selected from halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;

5 as well as pharmaceutically acceptable salts, hydrates, isoforms and/or optical isomers thereof.

2. A compound of formula I



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wherein

R<sup>1</sup> is selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by C<sub>1</sub>-C<sub>4</sub> alkyl;

15

R<sup>2</sup> is selected from hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>3</sup> is selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, F, CF<sub>3</sub>, CHF<sub>2</sub> and CH<sub>2</sub>F;

R<sup>4</sup> is selected from hydrogen, F, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F and CH<sub>3</sub>;

R<sup>5</sup> is selected from hydrogen and F;

R<sup>6</sup> is selected from hydrogen and F;

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Y<sup>1</sup> is selected from hydrogen, halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;

Y<sup>2</sup> is selected from hydrogen, halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;

Y<sup>3</sup> is selected from hydrogen, halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;

with the proviso that when Y<sup>1</sup> is hydrogen, Y<sup>2</sup> is selected from halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;

as well as pharmaceutically acceptable salts, hydrates, isoforms and/or optical isomers thereof.

3. A compound according to formula I of claim 1 or 2, wherein

5 R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>2</sup> is hydrogen;

R<sup>3</sup> is selected from hydrogen and C<sub>1</sub>-C<sub>2</sub> alkyl;

R<sup>4</sup> is hydrogen;

R<sup>5</sup> is hydrogen;

10 R<sup>6</sup> is hydrogen;

Y<sup>1</sup> is selected from hydrogen, chloro, C<sub>1</sub>-C<sub>2</sub> alkoxy, and C<sub>1</sub>-C<sub>2</sub> alkyl; and

Y<sup>2</sup> is selected from hydrogen, chloro, C<sub>1</sub>-C<sub>2</sub> alkoxy, and C<sub>1</sub>-C<sub>2</sub> alkyl;

with the proviso that when Y<sup>1</sup> is hydrogen, Y<sup>2</sup> is selected from chloro, C<sub>1</sub>-C<sub>2</sub> alkoxy, and C<sub>1</sub>-C<sub>2</sub> alkyl; and

15 Y<sup>3</sup> is hydrogen.

4. A compound according to claim 1 selected from;

2-[3-(3-methoxyphenoxy)prop-1-yn-1-yl]-6-methylpyridine;

2-[3-(3-methoxyphenoxy)prop-1-yn-1-yl]pyridine;

20 2-[3-(3-chlorophenoxy)but-1-yn-1-yl]-6-methylpyridine;

2-Methyl-6- (3-p-tolyloxy-prop-1-ynyl)-pyridine;

2-[3-(2,3-Dichloro-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

2-[3-(2,3-Dimethyl-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

2-[3-(2,3-Dimethyl-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

25 2-[3-(2,4-Dichloro-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

2-[3-(2,4-Dimethyl-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

2-[3-(2,5-Dichloro-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

2-[3-(2,5-Dimethyl-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

2-[3-(2,6-Dimethyl-phenoxy)-prop-1-ynyl]-6-methyl-pyridine;

30 2-Methyl-6- [3-(2-trifluoromethyl-phenoxy)-prop-1-ynyl]-pyridine;

2-[3-(2-Benzyl-oxo-phenyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(2-Bromo-4, 5-dimethyl-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(2-Chloro-4-methoxy-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(2-Chloro-5-methyl-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
5 2-[3-(2-Chloro-6-methyl-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-Methyl-6-(3-*o*-tolyl-oxo-phenyl)-prop-1-ynyl]-pyridine;  
2-Methyl-6-[3-(3,4,5-trimethyl-phenoxyl)-prop-1-ynyl]-pyridine;  
2-[3-(3,4-Dichloro-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(3,4-Dimethoxy-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
10 2-[3-(3,4-Dimethyl-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(3,5-Dichloro-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(3,5-Dimethoxy-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(3,5-Dimethyl-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-[3-(3-Bromo-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
15 3-[3-(6-Methyl-pyridin-2-yl)-prop-2-ynyl-oxo]-benzonitrile;  
2-[3-(3-Ethyl-phenoxyl)-prop-1-ynyl]-6-methyl-pyridine;  
2-methyl-6-[3-(3-methylphenoxyl)prop-1-yn-1-yl]pyridine;  
2-[3-(4-chloro-2-methylphenoxyl)prop-1-yn-1-yl]-6-methylpyridine;  
2-[3-(4-chloro-3,5-dimethylphenoxyl)prop-1-yn-1-yl]-6-methylpyridine;  
20 2-[3-(4-chloro-3-methylphenoxyl)prop-1-yn-1-yl]-6-methylpyridine;  
2-[3-(4-chlorophenoxy)prop-1-yn-1-yl]-6-methylpyridine;  
2-[3-(4-methoxyphenoxyl)prop-1-yn-1-yl]-6-methylpyridine;  
2-methyl-6-[3-(4-nitrophenoxy)prop-1-yn-1-yl]pyridine;  
2-methyl-6-[3-(3-nitrophenoxy)prop-1-yn-1-yl]pyridine;  
25 2-methyl-6-[3-(3-methylphenoxyl)prop-1-yn-1-yl]pyridine;  
2-methyl-6-[3-(5,6,7,8-tetrahydronaphthalen-2-yl-oxo)prop-1-yn-1-yl]pyridine;  
2-[3-(4-isopropylphenoxyl)prop-1-yn-1-yl]-6-methylpyridine;  
2-[3-(4-*tert*-butylphenoxyl)prop-1-yn-1-yl]-6-methylpyridine;  
6-[3-(3,4-dimethylphenoxyl)prop-1-yn-1-yl]-3-fluoro-2-methylpyridine; and  
30 6-[3-(3,4-dimethylphenoxyl)but-1-yn-1-yl]-3-fluoro-2-methylpyridine.

5. A compound according to any one of claims 1-4 for use in therapy.

6. A compound according to claim 5, wherein the therapy is treatment or prevention  
5 of gastroesophageal reflux disease.

7. Use of a compound according to formula I of claim 1 or 2, or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for the inhibition of transient lower esophageal sphincter relaxations.

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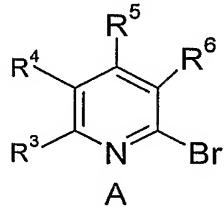
8. Use of a compound according to formula I of claim 1 or 2, or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for treatment or prevention of gastroesophageal reflux disease.

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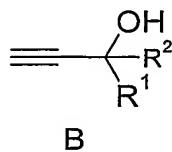
9. A pharmaceutical composition comprising a compound of formula I of claim 1 or 2 as an active ingredient, together with a pharmacologically and pharmaceutically acceptable carrier.

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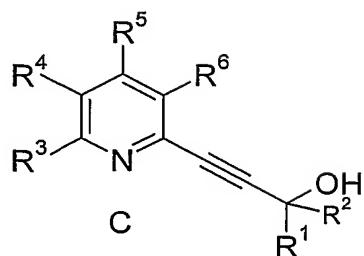
10. A process for the preparation of a compound of formula I, whereby a coupling reaction of the aryl bromide A



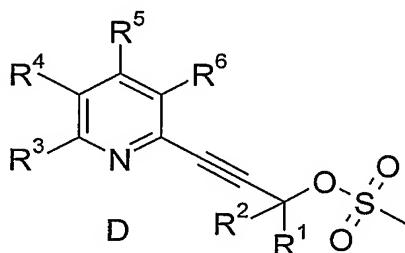
and the alcohol B



25 is performed in the presence of a base such as triethyl amine to give the alcohol C



which is then converted into the mesylate D



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and reacted with an alcohol, and wherein

R<sup>1</sup> is selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>2</sup> is selected from hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

10 R<sup>3</sup> is selected from hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, F, CF<sub>3</sub>, CHF<sub>2</sub> and CH<sub>2</sub>F;

R<sup>4</sup> is selected from hydrogen, F, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F and CH<sub>3</sub>;

R<sup>5</sup> is selected from hydrogen and F;

R<sup>6</sup> is selected from hydrogen and F.

15 11. A compound selected from 3-(5-fluoro-6-methylpyridin-2-yl)prop-2-yn-1-ol; 4-(5-fluoro-6-methylpyridin-2-yl)but-3-yn-2-ol; 3-(5-fluoro-6-methylpyridin-2-yl)prop-2-yn-1-yl methanesulfonate; 3-(5-fluoro-6-methylpyridin-2-yl)-1-methylprop-2-yn-1-yl methanesulfonate; 4-(6-methylpyridin-2-yl)but-3-yn-2-ol; and Methanesulfonic acid 1-methyl-3-(6-methyl-pyridin-2-yl)-prop-2-ynyl ester.

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12. A method for the inhibition of transient lower esophageal sphincter relaxations whereby an effective amount of a compound of formula I of claim 1 or 2 is administered to a subject in need of such inhibition.

5 13. A method for the treatment or prevention of gastroesophageal reflux disease, whereby an effective amount of a compound of formula I of claim 1 or 2 is administered to a subject in need of such treatment or prevention.